Coordination of growth and cell division by the TORC1 nutrient signaling pathway in *Saccharomyces cerevisiae*

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Living organisms coordinate cell growth with cell division in response to the availability of essential nutrients. Upon nutrient deprivation, cells arrest cell cycle progression in late G1 and enter into a reversible non-dividing but metabolically active state known as quiescence or G0. Under unfavorable conditions, failure to entry appropriately into this quiescent state may result in DNA replication and chromosome segregation errors and therefore loss of viability. In multicellular organisms, improper control of entry into and exit from quiescence may lead to uncontrolled proliferation and ultimately to tumor development.

In the yeast *Saccharomyces cerevisiae* several nutrient signaling pathways coordinate cell growth and division in response to nutrient availability. The work presented in this manuscript is focused on the master regulator of cell growth the Target Of Rapamycin Complex 1 (TORC1). Following starvation, inactivation of TORC1 results in the activation of the protein kinase Rim15, which orchestrates most aspects of the G0 program including proper G1 arrest. Rim15 controls most of its downstream readouts by inhibiting (indirectly via the yeast endosulfines Igo1/2) the protein phosphatase PP2ACdc55. Although many efforts have been made in deciphering the molecular mechanisms by which TORC1 regulates cell proliferation, many questions still need to be addressed. The aim of this thesis is to understand whether the TORC1-Rim15-Igo1/2-PP2ACdc55 signaling pathway impinges on G1 cell cycle events and if positive, to elucidate the underlying molecular mechanisms.

Combined, the findings of this thesis show that the TORC1-Rim15-Igo1/2-PP2ACdc55 signaling pathway controls cell cycle progression at the G1/S transition in response to nutrient availability by several mechanisms that impinge on key cell cycle regulators.

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